

REMARKS

Claims 1 – 6, 22, 24, 26, 27, 35, and 36 are currently pending. Claims 1, 22 and 24 are the pending independent claims. In the Office Action, Claims 1 – 6, 22, 24, 26, 27, 35, and 36 were rejected under Section 112, first paragraph as allegedly failing to satisfy the written description requirement. Claims 1 – 6, 22, 24, 26, 27, 35, and 36 were also rejected und Section 102 (c) as allegedly anticipated by U.S. Patent Application Publication No. 2005/0272720 to Keltjens et al.

All rejections are respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. **Written Description Rejections.**

The Examiner contends that Claims 1 – 6, 22, 24, 26, 27, 35, and 36 include new matter and therefore fail to satisfy the written description requirement.

First, the Examiner contends that several limitations in Claim 1 are not described in the specification, namely: (a) includes the formation of an “aqueous solution” in step i); (b) the adjustment of the pH of the “aqueous solution” in step ii); (c) the extraction of olanzapine from the “aqueous phase” in step iii); and (d) concentration of the solution to “form olanzapine salt crystals” in step iv). In response, the Applicants have amended Claim 1 to clarify the language and to more closely correspond to the language of originally filed Claim 7, which clearly is not new matter.

In addition, the Examiner alleges that the limitation “one or more” in Claims 2, 3, 4, and 6 constitutes impermissible new matter. While Applicants disagree with the assertion that the limitation “one or more” amounts to new matter in these claims, the limitation in question has been removed from Claims 2, 3, 4, and 6 in order to eliminate this issue and advance prosecution of the case.

The Examiner also objects to the limitation “mixtures thereof” in step ii) of claim 22 on the ground that it is allegedly not described in the specification. In response, this limitation has been deleted from the claim.

In regard to Claim 24, the Examiner contends that the limitation of providing separable “aqueous” and organic phase in step c) is not described in the specification. The Examiner also asserts that the limitation of neutralizing the “aqueous phase” in step d) is not described in the specification. In response, Claim 24 has been amended to clarify that a chlorinated organic solvent is added to the reaction mixture and that the water and organic solvent phases are then separated. In addition, Claim 24 has been amended in step d) to change “aqueous phase” back to the original “water phase.”

Finally, the Examiner alleges that the limitation “detectable” in Claims 35 and 36 is also impermissible new matter. Here again, Applicants disagree, but have nonetheless removed the term from Claims 35 and 36 in order to advance prosecution of the case.

In view of these amendments, it is submitted that any alleged written description issues have been overcome that the claims as amended are fully compliant with Section 112, and that all rejections under Section 112 should therefore be withdrawn.

II. Prior Art Rejections.

The Examiner contends that Claims 1 – 6, 22, 24, 26, 27, 35, and 36 are anticipated by Keltjens ‘720. It is respectfully submitted that these rejections are not well taken.

Independent Claims 1, 22, and 24 each call for specific steps in a process in which olanzapine is purified by first converting the olanzapine into an acid addition salt, which is then transformed back to olanzapine. In accordance with certain embodiments, this transformation is carried out by: i) dissolving an acid addition salt of olanzapine in water, ii) adjusting the pH of the solution to about 8-10, iii) extracting olanzapine from the water phase to an organic solvent phase and iv) isolating the acid addition salt of olanzapine from the organic solvent phase by concentrating the solution and separation of the crystals of the aforementioned salt of olanzapine therefrom. Applicants have determined this process enables significant reductions in the amount and nature of undesired impurities in the final olanzapine product. In particular, Applicants have determined that the process enables production of olanzapine containing less than 0.05 % of the impurity piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5] benzodiazepine.

Contrary to the Examiner's assertions, Applicants' process is not disclosed or suggested by the Keltjens '720 disclosure. Keltjens says nothing about the impurity piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5] benzodiazepine. Keltjens does not even recognize the existence of this impurity, much less teach a method for substantially removing the impurity from olanzapine via conversion to the acid addition salt and then transformation back to olanzapine.

The focus of Keltjens '720 is to make what is said to be a special, novel form of olanzapine, namely olanzapine acetate, which is also said to yield a relatively stable pure olzapine Form I (as defined therin) simply by heating. Except for making the alleged novel olanzapine acetate, Keltjens '720 does not purport to disclose a new way of synthesizing olanzapine per se or using the acid addition salt thereof in the manner of Applicants' claimed invention to provide an olanzapine product with very little or no detectable amount of noted piperazine impurity compound. The Examiner has not shown how Applicants' claimed method is described in or would have been obvious from Keltjens '720 and its totally different focus on making olanzapine acetate and the ensuing heating process to make what is alleged to be substantially pure olanzapine Form I. This is far from what Applicants claim.

Thus, the anticipation rejections based on the Keltjens '720 reference are not well taken and should be withdrawn.

In light of the foregoing, the present amendment is believed to place the application in a condition for allowance. Entry of the foregoing amendments to the claims and allowance of all pending claims is respectfully solicited.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our **Deposit Account No. 12-2355**.

Respectfully submitted,

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